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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,618	04/14/2005	Kirvin L Hodge	18034-PCTUS	8180

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EXAMINER	
ZHANG, NANCY L	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 11/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/531,618	HODGE ET AL.	
	Examiner	Art Unit	
	Nancy L. Zhang	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-22 and 24-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-22 and 24-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 07/19/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 6-22 and 24-29 are pending and examined.

Lack Scope of Enablement Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-22 and 24-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing blood glucose, triglycerides and fatty acids level in diabetic mice using 4-(3-(2,6-dimethylbenzyloxy)-phenyl)-4(R)-hydroxybutanoic acid – one compound of formula (I), does not reasonably provide enablement for treating all of the diseases listed in claim 6 using any compound of formula (I). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described in ***In re Wands***, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: the nature of the invention; the state of the prior art; the relative skill of those in the art; the predictability or unpredictability of the art; the breadth of the claims; the amount of direction or guidance presented; the presence or absence of working examples; and the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's

position that one skilled in the art could not practice the invention without undue experimentation.

The present invention are drawn to a composition comprising a biologically active compound of formula (I) and a method for treating insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver disease, cachexia, obesity, atherosclerosis and arteriosclerosis by administering the composition to a mammalian subject such as a human.

The specification only discloses that a compound of the formula (I) 4-(3-(2,6-dimethylbenzyloxy)-phenyl)-4(R)-hydroxybutanoic acid as an example exhibits biological activity for reducing blood glucose, triglycerides and fatty acids level in diabetic mice.

It is generally recognized in the art that biological compounds often react unpredictably under different circumstances (Nationwide Chem. Corp. v. Wright, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970)). The relative skill of the artisan or the unpredictability of the pharmaceutical art is very high. Where the physiological activity of a chemical or biological compound is considered to be an unpredictable art (Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved" (See In re fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970)), the skilled artisan would have not known how to extrapolate the result provided in the instant specification to the larger and highly varied genus of using

the compounds of formula (I) for the treatment of all of the disorders including insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver disease, cachexia, obesity, atherosclerosis and arteriosclerosis. For example, cachexia is characterized by progressive weakness, dramatic weight loss and wasting and is a common condition arising in many human cancer patients (Tisdale et al., US Patent 5,219,579, issued Jun. 15, 1993, column 1, lines 26-28). The specification of the instant application has not provided guidance, working example or mechanisms of action for the treatment of cachexia using the compounds of formula (I).

The examiner acknowledges that the Office does not require the presence of working examples to be present in the disclosure of the invention (see MPEP 2164.02). However, given the highly unpredictable state of the art and furthermore, given that the applicant does not provide sufficient guidance or direction as to how to make and use the full scope of the instant claimed invention without undue amount of experimentation, the Office would require appropriate disclosure, in the way of scientifically sound reasoning or the way of concrete examples, as to why the data shown is a reasonably representative and objective showing such that it was commensurate in scope with and, thus, adequately enables, the use of the compounds of formula (I) for the full scope of the presently claimed subject matter. In the absence of such guidance and evidence or reasoning, the specification fails to provide an enabling disclosure.

Claim Rejections - 35 USC § 103

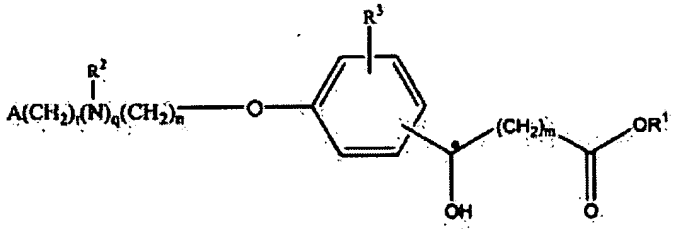
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6-22 and 24-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sharma et al. (WO 02/100341, pub. date: Dec. 19, 2002, item U on PTO 1449 filed Jul. 19, 2005) in view of Pischel et al. (US Patent 6,307,080, issue date: Oct. 23, 2001) and Mathieu et al. (US Patent 5,665,387, issue date: Sep. 9, 1997).

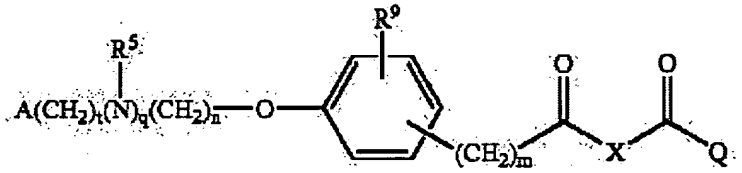
Claims 6-22 and 24-29 recite a composition comprising a biologically active compound of formula (I) and a method for treating insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver disease, cachexia, obesity, atherosclerosis and arteriosclerosis by administering the composition to a mammalian subject such as a human.



Formula I

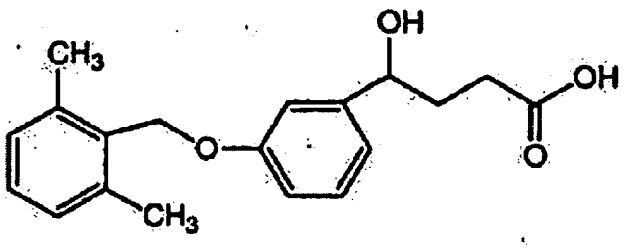
Sharma et al. disclose a compound of formula (I') (column 2, line 10):

I'

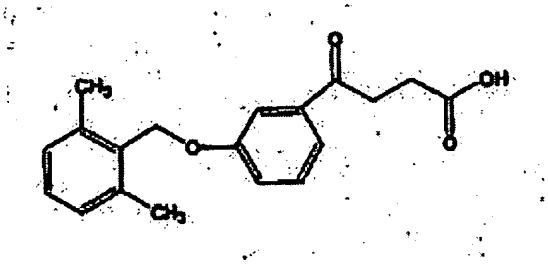


wherein n is 1 or 2; m is 0 or 1; q is 0 or 1; t is 0 or 1; R^5 is alkyl having from 1 to 3 carbon atoms; R^9 is hydrogen, halo, or alkoxy having from 1 to 3 carbon atoms; A is phenyl, unsubstituted or substituted by 1 or 2 groups selected from: halo, alkyl having 1 or 2 carbon atoms, perfluoromethyl, alkoxy having 1 or 2 carbon atoms, and perfluoromethoxy; or cycloalkyl having from 3 to 6 ring carbon atoms wherein the cycloalkyl is unsubstituted or one or two ring carbons are independently mono-substituted by methyl or ethyl; or a 5 or 6 membered heteroaromatic ring having 1 or 2 ring heteroatoms selected from N, S and O and the heteroaromatic ring is covalently bound to the remainder of the compound of formula I by a ring carbon; and X is $—CH_2—$, Q is $—OR^1$ and R^1 is ethyl; or X is $—CH_2CR^{12}R^{13}—$ or $—CH_2CH(NHAc)$-wherein each of R^{12} and R^{13} is independently hydrogen or methyl, Q is OR^1 and R^1 is hydrogen or alkyl having from 1 to 7 carbon atoms; or X is $—CH_2CH_2—$ and Q is $NR^{10}OR^{11}$ wherein one of R^{10} and R^{11} is hydrogen, alkyl having from 1 to 3 carbon atoms or hydroxy, and the other is hydrogen or alkyl having from 1 to 3 carbon atoms; or when R^1 is hydrogen, a pharmaceutically acceptable salt of the compound.

Claim 9 recites one biological active agent 4-(3-(2,6-dimethylbenzyloxy)-phenyl)-4(R)-hydroxybutanoic acid having the following structure:



Sharma et al. disclose one of the compounds of formula (I') is 4-(3-(2,6-dimethylbenzyloxy)-phenyl)-4-oxobutyric acid having the following structure (page 136, line 20):



Sharma et al. disclose that the compounds of formula (I') are biologically active agents useful for the treatment of insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver disease, cachexia, obesity, atherosclerosis and arteriosclerosis (see abstract). The base structure of formula (I') is the same as the base structure of formula (I) of the instant application. Sharma et al. further disclose that preferably the agent is administered orally (column 10, line 60) and that both human and non-human mammalian subjects can be treated (column 11, lines 49-50) for type II diabetes

(column 11, line 34) in an amount of 1 mg to 400 mg once or twice per day (column 11, lines 57-58).

The difference between the prior art compound and the compound of the instant application is the use of a hydroxyl group instead of a keto group next to the core benzene ring in the formula. However, a hydroxyl group and a keto group are analogous to each other. Pischel et al. (US Patent 6,307,080) disclose compounds for treating diabetes (see abstract) where the organic acid used can be any physiologically safe carboxylic acid which may be optionally substituted with keto or hydroxyl group (column 5, lines 7-10). Mathieu et al. (US Patent 5,665,387) also disclose compounds for treating diabetes where one of more carbon atoms of the R group may be replaced by hydroxyl or keto (column 3, line 11). Therefore, one having ordinary skill in the art would have been motivated to substitute the keto group of the prior compounds with a hydroxyl group to result in the compounds of the instant application with the expectation that the substitution would not significantly alter the analogous properties of compounds of the prior art due to close structural similarity of the compounds. See In re Grunwell, 203 USPQ 1055.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 6-22 and 24-29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6-22 of copending Application No. 10/553,936, claims 6-22 of copending Application No. 10/554,586 and claims 1-66 of copending Application No. 11/535,779 in view of Reiffen et al. (US Patent 5,604,225, issue date: Feb. 18, 1997), Talley et al. (US Patent 6,156,781, issue date: Dec. 5, 2000), Mathieu et al. (US Patent 5,665,387, issue date: Sep. 9, 1997) and Griffin (US PGPub 2002/0028943, pub date: Mar. 7, 2002). Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

With respect to claims 6-22 of copending Application No. 10/553,936, the base structure of formula (I) is the same as the base structure of formula (I) of the instant application. Furthermore, the physiological activities are analogous. The only difference is that there is a hydroxyl group adjacent to the benzene ring on the carbon chain of the alkyloic acid in the formula of the instant application whereas there is a double bond instead of a hydroxyl group at the same position in the formula of the

copending application. However, Reiffen et al. (US Patent 5,604,225) disclose compounds useful in the treatment of diabetes (see abstract) where the R_4 group can be selected from the group including hydroxyl and alkenyl (column 2, lines 7-11). Talley et al. (US Patent 6,156,781) also disclose compounds useful for the treatment of diabetes (column 4, line 59) where the R^4 group can be optionally substituted at a substitutable position with hydroxyl or alkenyl (column 14, line 11). One having ordinary skill in the art would have been motivated to substitute the hydroxyl group with a double bond with the expectation that the substitution of a hydroxyl group for a double bond would not significantly alter the analogous properties of the compound due to close structural similarity of the compounds. See In re Grunwell, 203 USPQ 1055.

With respect to claims 6-22 of copending Application No. 10/554,586, the base structure of formula (I) is the same as the base structure of formula (I) of the instant application. Furthermore, the physiological activities are analogous. The only difference is that there is a hydroxyl group adjacent to the benzene ring on the carbon chain of the alkyloic acid in the formula of the instant application whereas there is no hydroxyl group at the same position in the formula of the copending application and there is a keto group at the α position of the alkyloic acid. However, keto, hydroxyl and alkyl are common substitutuents to each other. Griffin (US PGPub 2002/0028943) discloses substituted alkyl can be alkyl (page 7, paragraph [0155], line 1), hydroxyl or keto (page 8, left column, line 3). Mathieu et al. (US Patent 5,665,387) also disclose compounds for treating diabetes where one of more carbon atoms of the R group may be replaced by alkyl or hydroxyl or keto (column 13, lines 27-28). One having ordinary

skill in the art would have been motivated to substitute alkyl, hydroxyl and keto with each other with the expectation that the substitution would not significantly alter the analogous properties of the compound due to close structural similarity of the compounds. See In re Grunwell, 203 USPQ 1055.

With respect to claims 1-66 of copending Application No. 11/535,779, the base structure of formula (I') is the same as the base structure of formula (I) of the instant application. Furthermore, the physiological activities are analogous. The only difference is that there is a hydroxyl group adjacent to the benzene ring on the carbon chain of the alkyloic acid in the formula of the instant application whereas there is no hydroxyl group at the same position in the formula of the copending application and there is a keto group at variable positions of the alkyloic acid. However, keto, hydroxyl and alkyl are common substitutuents to each other. Griffin (US PGPub 2002/0028943) discloses substituted alkyl can be alkyl (page 7, paragraph [0155], line 1), hydroxyl or keto (page 8, left column, line 3). Mathieu et al. (US Patent 5,665,387) also disclose compounds for treating diabetes where one of more carbon atoms of the R group may be replaced by alkyl or hydroxyl or keto (column 13, lines 27-28). One having ordinary skill in the art would have been motivated to substitute alkyl, hydroxyl and keto with each other with the expectation that the substitution would not significantly alter the analogous properties of the compound due to close structural similarity of the compounds. See In re Grunwell, 203 USPQ 1055.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy L. Zhang whose telephone number is (571)-272-8270. The examiner can normally be reached on Mon.- Fri. 8:30am - 5:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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PRIMARY EXAMINER